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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,881	09/11/2003	Harlan W. Waksal	1017.33492.US3	8515

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,881	WAKSAL ET AL.	
	Examiner	Art Unit	
	ANNE HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,3,24 and 31-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 24 and 31-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 4/14/2008 is acknowledged. Clams 49-73 were added

Claims 1, 3, 24 and 31-73 are pending and examined on the merits.

Claim Rejections Withdrawn:

The provisional rejection of claims 1,3, 24 and 31-48 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 11/206,825 is withdrawn in view of the abandonment of application no. 11/206,825.

Claim Rejections Maintained and New Grounds of Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 64, 65, 69-71 and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 64, 65, 69-71 and 73 were entered with the amendment filed 4/14/2008. Applicants point to page 19, line 7 to page 20, line 15 for support for this amendment. Claims 64 and 65 are drawn to methods, wherein the radiation is administered at a dose of between 65 and 80 Gy or a dose that is selected from the group consisting of 15 Gy, 20 Gy and 35 Gy. The specification (page 8, lines 22- 23) teaches that doses such as 35 Gy, 15 Gy, 20 Gy or 65-80 Gy are reported to have been administered to particular organs. This teaching by the specification fails to provide support for the claimed methods of treating cancer comprising administering an antibody that binds EGFR in combination with radiation for the purpose of inhibiting the growth of a tumor of the beast, lung, colon, kidney, bladder, head and neck, ovary, prostate or brain. The reference in the specification of the particular radiation doses recited in claims 64 and 65 is not taught in the context of treating cancer in combination with an anti-EGFR antibody. Therefore, the cited passage of the specification does not provide support for the methods of claims 64 and 65.With respect to claims 69, 70 or 73, these claims depend from claim 68, which is drawn to a method of treating head and neck cancer comprising the administration of the C225 antibody with a particular dose of 250 mg/m_2, where the c225 antibody is administered before radiation, or before and during radiation. The specification does not provide support for these particular embodiments of claims 69, 70 or 73. The passage pointed to by applicants does not identify the cancer that is treated, and only refers to treating cancer patients with the C225 antibody along with radiation, and does not teach that the antibody was administered "before and during" the radiation; or that the antibody was administered "before" radiation. Therefore, the specific embodiments of claims 69, 70 and 73 appear to be drawn to narrow embodiments that were not originally contemplated at the time the invention was filed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3, 24, 31, 32, 34, 38, 45, 49-63, 66-70 and 72 remain/are rejected under 35 U.S.C. 102(a) as being anticipated by Ezekiel (Proceedings of ASCO, 17: Abstract No. 1522, 1998, April 15; cited in IDS). This rejection is applied to new claims 49-63, 66-70 and 72.

Applicants' arguments have been carefully considered, but fail to persuade. Applicants state that the present application is entitle to the priority benefit of US application no. 60/085,613 filed May 15, 1998, and that Ezekiel was published less than one year before this date. Applicants further state that inventors Waksal, Saleh, Robert (no mention of Buchsbaum, also a named inventor for this application) are co-authors of Ezekiel, and that accordingly the rejection should be withdrawn. This is not persuasive because it is the inventive entity that is compared with the prior art when making a rejection under 35 USC 102(a), not whether there are common inventors between an application and an applied reference. In the instant case the inventive entity of the present application is Waksal, Saleh, Robert and Buchsbaum. The inventive entity for Ezekiel is Ezekiel, Robert, Meredith, Spencer, Newsome, Khazaeli, Peters, Saleh, Lobuglio and Waksal, which is a different inventive entity from that of the instant application. Therefore, Ezekiel does qualify as prior art under 35 USC 102(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 24, 31-39, 41, 43, 45, 47 and 49-73 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos (ASCO Annual Meeting, Abstract No. 1381, 1996) in view of Saleh (Saleh, M. et al., Proceedings of the American association for Cancer Research,

37: 612, Abstract #4197, 1996, March; cited in the IDS). This rejection applies to new claims 49-73.

Claims 1, 3, 24, 31-41, 43-47 and 49-67 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos (ASCO Annual Meeting, Abstract No. 1381, 1996) in view of Saleh (Saleh, M. et al., Proceedings of the American association for Cancer Research, 37: 612, Abstract #4197, 1996, March; cited in the IDS), and further in view of Goldstein (Goldstein, N.I. et al, Clinical Cancer Research, 1: 1311-1318, 1995; cited in a previous Office action).

Claims 1, 3, 24, 31-39, 41-43, 45, and 47-73 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos (ASCO Annual Meeting, Abstract No. 1381, 1996) in view of Saleh (Saleh, M. et al., Proceedings of the American association for Cancer Research, 37: 612, Abstract #4197, 1996, March; cited in the IDS), and further in view of Arnold (U.S. 5,736,534; issued April 7, 1998; effective filing date July, 29, 1996; cited in the IDS).

Response to Arguments:

The separate rejections under 35 USC 103(a) are argued together by applicant. Applicants' arguments have been carefully considered, but fail to persuade. Applicants argue that that the present claims are non-obvious over the cited references, because of a secondary indicia of non-obviousness, that of synergy between C225 and radiation. Applicants provide Huang and Harari, as well as Bianco for consideration, and assert that these references provide evidence that there is a synergistic effect of combining C225 administration with radiation

treatment. This is not found persuasive, because synergy itself is not a secondary indicia of non-obviousness, rather it is synergy where synergy is a surprising result. In the instant case, even if the Huang and Harari, and Bianco references establish that there is synergy between C225 administration and radiation treatment, it does not appear that the teachings of Huang and Harrari, nor that of Bianco, provide evidence that this synergy is a surprising result of combining the C225 antibody with radiation treatment. The Huang and Harari reference teaches that preliminary findings have suggested that EGFR blockade might enhance anti-tumor responses (se page 2166, right column). The Bianco reference teaches that prior to the publication date of Bianco it was known that radiation treatment resulted in increased expression of survival pathways that could be blocked by an EGFR inhibitor such as C225 (see page 4343, right column, and page 4349, left column). Additionally, the Saleh (cited in the previous rejections) teaches that a combination of radiation and an anti-EGFR antibody resulted in an increase in efficacy of treating tumors. Thus, applicants have failed to provide evidence that a synergistic effect of combining an EGFR inhibitor such as the C225 antibody with radiation therapy is a surprising result. Furthermore, there is no evidence in the specification that the combination of the C225 antibody with radiation treatment produced a surprising result of synergy between the two treatments. Therefore, the rejections are maintained for the reasons of record.

Conclusion

No claim is allowed. Although claims 51-58, 61, and 66-73 require the use of a specific antibody, C225, no rejection under 35 USC 112, first paragraph is made because the structure of this antibody is disclosed in the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
July 21, 2008

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643